FACT SHEET
Healthcare Provider

Glutaric Acidemia Type I (GA I)

Description:
Glutaric acidemia, type I (GA-I) is an autosomal recessive inborn error of metabolism caused by the deficiency of glutaryl-CoA dehydrogenase, an essential enzyme in the catabolism of the amino acids tryptophan, lysine, and hydroxylysine. Some infants are symptomatic early, while in others the disorder may appear suddenly and present as a toxic encephalopathy after a period of apparently normal development.

Incidence in General Population:
1:75,000 live births

Symptoms:
This enzyme deficiency disorder is characterized by hypoglycemia, dystonia, and dyskinesia. Symptoms include vomiting, poor feeding, neurologic symptoms such as seizures and abnormal tone, and lethargy progressing to coma. Additional neurologic findings may include repetitive movements or abnormal posturing. Despite slow improvement, many patients do not fully recover from a neurologic crisis.

The most significant physical sign in GA-I is macrocephaly; in fact, macrocephaly may be the only physical sign in otherwise asymptomatic infants. Macrocephaly is present at or shortly after birth in 70% of infants who have GA I. Most commonly, infants develop progressive macrocephaly with markedly accelerated rates of head circumference growth in the first few months of life.

There are several different clinical presentations:
1. Affected infants appear normal and then suffer an acute metabolic crisis, usually 6 and 18 months of age, with subsequent neurological findings that improve slightly and then remain static. Changes in the basal ganglia, in particular atrophy of the caudate and putamen, develop within a few days or weeks of the encephalopathic episode. Neuronal loss and fibrous gliosis occur in the caudate and putamen as part of neurotoxicity of GA I.
2. Infants have a period of normal development, acute crisis, and subsequent neurological findings similar to those above, then progress slowly with recurrent episodes of ketosis, vomiting, hepatomegaly, and encephalopathy when the child develops infections.
3. Approximately 25% of infants gradually develop motor delay, hypotonia, dystonia, and dyskinesis during the first few years of life without any apparent acute crisis. Individuals can be completely asymptomatic without any crises and have normal development.

Neuroradiographic findings of frontal-temporal atrophy and/or arachnoid cysts before the onset of symptoms may be seen. Infants with GA-I are prone to suffer acute subdural hemorrhages and retinal hemorrhages after minor head trauma, i.e., commonly around the first birthday when starting to walk. This can be misdiagnosed as child abuse. In this population, 20-39% of patients have “chronic” subdural effusions and hematomas identified on neuroimaging studies; these are always found in the presence of atrophy and extra cerebral fluid.

Diagnosis:
Newborn screening abnormality—Tandem mass spectrometry: increased C5DC.
A second dried blood spot filter paper card may be requested by the Newborn Screening Laboratory if the initial screening result is above the normal range. Infants with presumptive positive screening (critical) results require prompt follow up. If this occurred, the clinician would be contacted by the Metabolic

Treatment Center. When notified of these results, the clinician should immediately check on the clinical status of the baby and facilitate referral to the Metabolic Treatment Center. The Metabolic Treatment Center will provide consultation and assistance with diagnostic testing.

Situations That Risk Metabolic Decompensation:
Fasting, intercurrent illness, post vaccination, and surgery.

Monitoring:
Clinical observation is the most important tool for monitoring patients with GA-I. It is important for the primary care provider and the Metabolic Treatment Center to develop an ongoing collaborative relationship in caring for these patients.

Treatment:
- Restricting dietary lysine and tryptophan rather than restricting total protein allows a greater intake of overall nitrogen.
- Pharmacologic doses of riboflavin, which serves as a cofactor for glutaryl-CoA dehydrogenase and facilitates any residual enzyme activity.
- Carnitine supplementation has been shown to increase the urinary excretion of glutaric acid and replenish reduced body carnitine stores.
- During an acute neurologic crisis, additional protein restriction and carbohydrate supplementation are introduced to prevent or reverse endogenous protein catabolism.
- The parents should have an emergency protocol with them at all times. This protocol can be provided by the Metabolic Treatment Center, and it should contain basic information about the disorder, necessary diagnostic investigations, and guidelines for treatment.
- Infants and children with GA-I should have regularly scheduled visits at the Metabolic Treatment Center.

Illness and Immunizations:
Intercurrent illnesses and vaccinations may aggravate hypotonia, unusual hand movements, and posturing but are usually reversible and of little clinical significance though they may precipitate crises (usually after the first birthday). Prevention and/or early intervention are of particular importance. For this and other reasons **immunizations must be kept on track**. There is no contraindication to immunization because of GA-I, but patients and physicians should be alerted to the need for immediate evaluation if high fever, lethargy, or vomiting occurs in the first 24 hours. The Metabolic Treatment Center should be consulted within 24 hours of the onset of the illness. Influenza vaccinations are also recommended.

Surgical/Surgical Procedures:
Preoperative fasting can precipitate encephalopathic crises.

Growth and Development:
Some patients may be intellectually intact; however, capabilities are dependent on avoidance of metabolic decompensation.

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